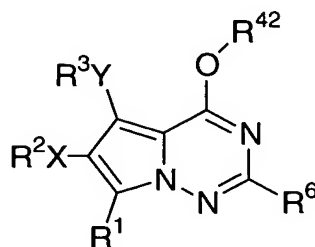


What is Claimed is:

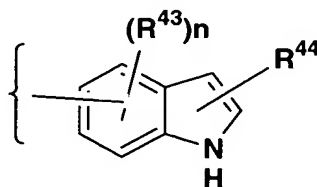
1. A process for preparing a compound of formula (I)



(I)

wherein

- X and Y are independently selected from O, OCO, S, SO, SO₂, CO, CO₂, NR¹⁰, NR¹¹CO, NR¹²CONR¹³, NR¹⁴CO₂, NR¹⁵SO₂, NR¹⁶SO₂NR¹⁷, SO₂NR¹⁸,
 10 CONR¹⁹, halogen, nitro, cyano, or X or Y are absent;
 R¹ is hydrogen;
 R² and R³ are independently hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, heterocyclo, substituted heterocyclo, aralkyl, substituted aralkyl, heteroaryl, substituted heteroaryl,
 15 heterocycloalkyl or substituted heterocycloalkyl; with the proviso that when X is halo, nitro or cyano, R² is absent, and, when Y is halo, nitro or cyano, R³ is absent;
 R⁶ is H;
 R⁷, R⁸, R⁹, R¹⁰, R¹¹, R¹², R¹³, R¹⁴, R¹⁵, R¹⁶, R¹⁷, R¹⁸ and R¹⁹ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl,
 20 substituted aryl, heteroaryl, substituted heteroaryl, heterocyclo, or substituted heterocyclo;
 R⁴² is



$(R^{43})_n$ wherein n equals 0, 1 or 2 and each R^{43} is independently selected from the group consisting of hydrogen, fluorine, chlorine and methyl; and

R^{44} is methyl, or hydrogen,

5 with the further provisos that:

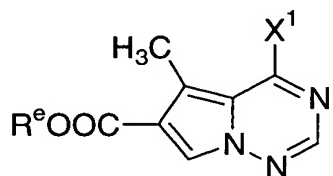
a. R^2 may not be hydrogen if X is SO, SO₂, NR¹³CO₂, or NR¹⁴SO₂; and

b. R^3 may not be hydrogen if Y is SO, SO₂, NR¹³CO₂, or NR¹⁴SO₂;

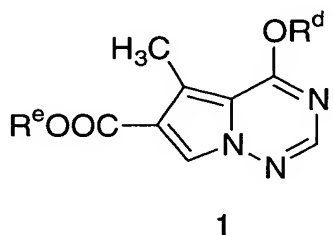
or an enantiomer, diastereomer, or pharmaceutically acceptable salt, prodrug, or solvate thereof,

10 which comprises the steps of

a) converting a compound of the formula



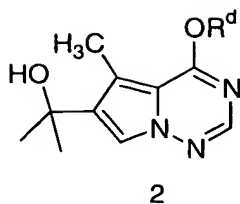
15 where R^e is lower alkyl or aryl and X^1 is a halogen to a compound 1 of the formula



where R^d is lower alkyl, aryl, substituted aryl, heteroaryl or substituted heteroaryl, by

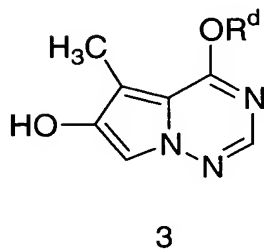
20 treatment with a phenoxide, or alkoxide,

b) alkylating Compound 1 to afford Compound 2 of the formula



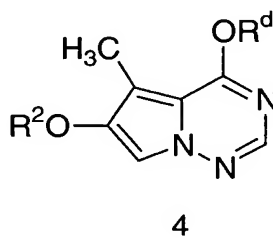
c) treating compound 2 with a peroxide in the presence of a Lewis acid to afford compound 3 of the formula

5



d) alkylating the phenol group in compound 3 to afford Compound 4 of the formula

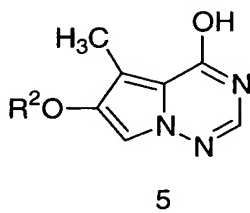
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where R² is benzyl or substituted benzyl,

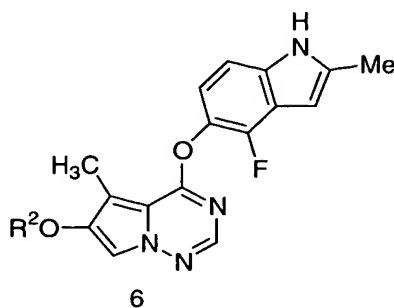
e) hydrolyzing Compound 4 to afford Compound 5 of the formula

15



where R^2 is benzyl or substituted benzyl, and

- f) converting Compound 5 to Compound 6 of the formula



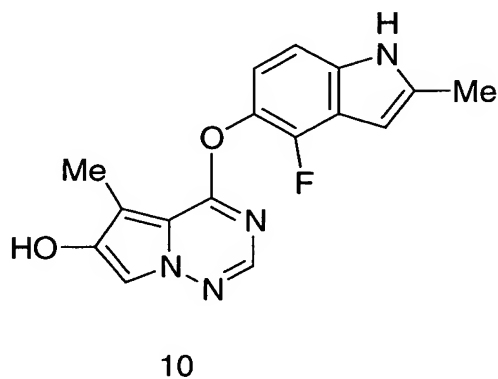
5

by first converting compound 5 to a chloroimidate, subsequently alkylating the chloroimidate to afford Compound 6 wherein R^2 is benzyl and deprotecting the phenol by treatment with a hydrogen donor in the presence of a catalyst to afford compound 6 where R^2 is hydrogen.

10

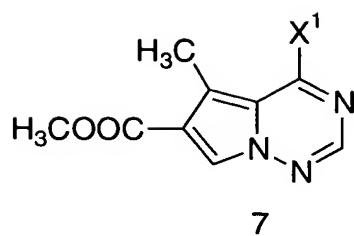
2. The process according to Claim 1 wherein in step c), hydrogen peroxide is used in the presence of a Lewis acid to convert the benzylic alcohol to the phenol.

- 15 3. A process for preparing a compound of the formula



which comprises the steps of

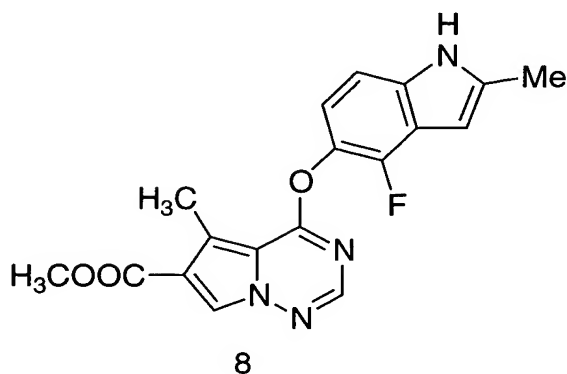
- 20 a) reacting a compound of the formula



where X_1 is halogen;

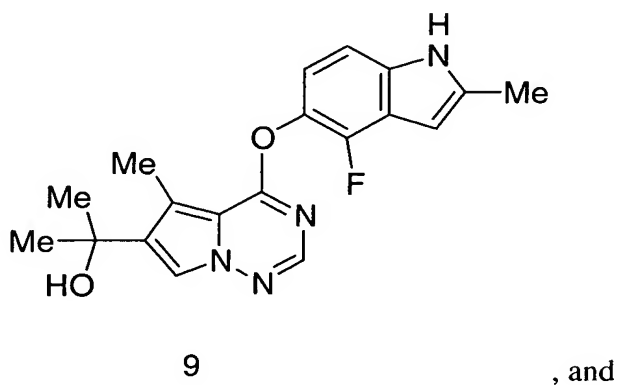
with a nucleophile to afford Compound 8 of the formula

5



b) treating Compound 8 with an alkylating agent at low temperature, to afford Compound 9 of the formula

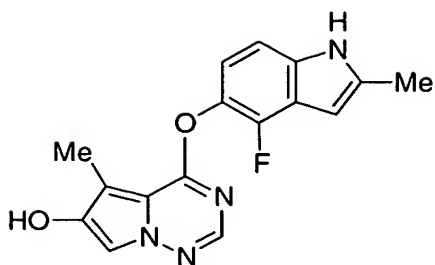
10



, and

c) treating Compound 9 with a peroxide in the presence of a Lewis acid to afford Compound 10 of the formula

15



10

4. The process according to Claim 3 wherein the alkylating agent in step (b) is an alkyl magnesium halide.

5

5. The process according to Claim 4 wherein the alkyl magnesium halide is methyl magnesium bromide or methyl magnesium chloride.

6. The process according to Claim 4 wherein the peroxide used in step c) is hydrogen peroxide or sodium perborate.

10

7. The process according to Claim 4 wherein the Lewis acid used in step c) is boron trifluoride.

15

8. A process for preparing a compound of the formula



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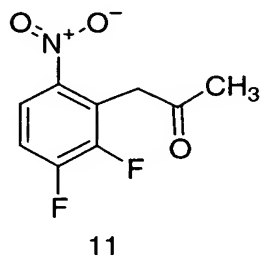
which comprises the steps of

20

a) reacting a fluorinated compound of the formula

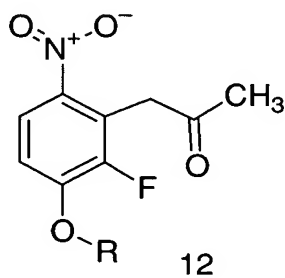


b) with a nucleophile to afford Compound 11 of the formula



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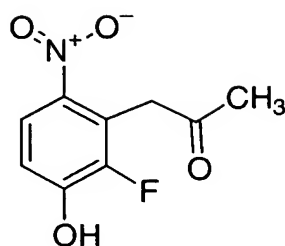
c) reacting Compound 11 with an alkoxy anion to afford Compound 12 of the formula



10

wherein R is a protecting group,

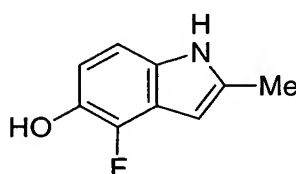
d) deprotecting the alkoxy group by treatments with deprotecting reagents
15 to afford Compound 13 of the formula



13 , and

e) cyclizing Compound 13 under reducing conditions to afford Compound 14 .

5



14

9. The process according to Claim 8 wherein the reduction in step (e) utilizes sodium dithionite in water or a mixture of water and an organic solvent such as THF.

10. The process according to Claim 8 wherein the reduction in step (d) utilizes pyridinium chloride or pyridinium iodide or hydrogen bromide.

11. A pharmaceutical composition comprising at least one or more compounds of Claim 1 in combination with a pharmaceutically acceptable carrier and at least one additional anti-cancer or cytotoxic agent.

12. A method for producing an antiangiogenic effect which comprises administering to a mammalian species in need thereof, an effective antiangiogenic producing amount of at least one compound made by the process of Claim 1.

13. A method for producing a vascular permeability reducing effect which comprises administering to a mammalian species in need thereof an effective vascular

permeability reducing amount of at least one compound made by the process of Claim 1.

14. A method of inhibiting protein kinase activity of growth factor receptors
5 which comprises administering to a mammalian species in need thereof, an effective protein kinase inhibiting amount of at least one compound made by the process of Claim 1.

15. A method of inhibiting tyrosine kinase activity of growth factor
10 receptors which comprises administering to a mammalian species in need thereof, an effective tyrosine kinase inhibiting amount of at least one compound made by the process of Claim 1.

16. A method for treating diseases associated with signal transduction
15 pathways operating through growth factor receptors, which comprises administering to a mammalian species in need thereof a therapeutically effective amount of at least one compound made by the process of Claim 1.